Radiological Aspects of "Collagen" Diseases

L. H. GARLAND, M.D., and M. A. SISSON, M.D., San Francisco

• *The collagen diseases, an ill-defined group of clinical entities, have as their basis a generalized alteration of the connective tissue, especially of its extracellular components. They include periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis, scleroderma, rheumatic fever and rheumatoid arthritis.*

The radiological findings in a series of cases of these diseases were reviewed.

In 28 cases of periarteritis, 20 cases showed some abnormal findings in the thorax. These included pleural effusions, pulmonary changes, pericardial effusions and cardiac enlargement.

In 32 cases of disseminated lupus erythematosus, thoracic findings were noted in 21. They resembled the changes found in periarteritis.

In some 25 cases of scleroderma, diverse radiological findings were noted. These included "cystic" changes in the lungs (one case) and pulmonary "hives." In the intestinal tract esophageal and small bowel alterations were found, both ectatic and stenotic. In the soft tissues of the "pressure areas" variable degrees of calcification were observed.

Dermatomyositis is the rarest of the collagen disease group; only one autopsy-proven case is available for study. Chest x-rays taken a year before death showed slight cardiac enlargement. The lungs were clear.

In acute rheumatic fever, x-ray examination may disclose pericardial or pleural effusion, and so-called rheumatic pneumonitis; the latter has no specific diagnostic features. Soft tissue swellings may develop around some of the joints.

In rheumatoid arthritis, joint changes are numerous and fairly characteristic, and are followed in many cases by fibrous or bony ankylosis and deformities of considerable degree.

Awareness of the commoner radiological changes in this entire group of diseases should result in earlier establishment of diagnosis, especially in the more obscure examples.

As EVOLUTION PROCEEDS, some diseases are conquered or become less common while others develop or become recognizable as separate entities. For some of the latter order a nomenclature is invented and the clarity of epithet is usually in direct proportion to the knowledge of etiologic delineation. Among diseases for which the nomenclature is as yet inept—for the reason indicated—are the so-called collagen diseases.

What are the collagen diseases? What are their radiologic aspects? What is ostensibly new concerning them? Some progress toward answers to some of these questions may be made by reviewing the cases of 86 patients with diagnosis of collagen disease who were observed in hospital practice during the last several years.

The collagen diseases are a group of disorders characterized anatomically by generalized alterations of the connective tissue, especially of its extracellular components. The following are currently accepted as members of this group: Periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis, scleroderma, rheumatic fever and rheumatoid arthritis.

The term *polyarteritis* is synonymous with *periarteritis nodosa.* Because of the predominance of vascular changes, this disorder (and, to a lesser extent, generalized lupus erythematosus) may also be referred to as *visceral angiitis.* Disseminated lupus erythematosus is also known as *acute lupus erythematosus* or *generalized lupus erythematosus.*

Becker[2] and others suggested that since the systemic manifestations of Schonlein-Henoch *purpura,* of *erythema nodosum* and of certain cases of *glomerulonephritis* show similar involvement of connective tissue, they too may belong to this group of diseases. Ehrick[4] and associates, on the basis of animal experiments, would also include *serum sickness.* Kampmeier[10] suggested that the necrotic changes found in afferent renal arteries in both malignant hypertension and periarteritis nodosa have more than coincidental relationship. Stewart[18] expressed belief that thromboangiitis obliterans and ulcerative colitis also are collagen diseases.

Presented before the Section on Radiology at the 82nd Annual Session of the California Medical Association, Los Angeles, May 24-28, 1953.

From the Department of Radiology, Stanford University Medical School Service, San Francisco Hospital.

ETIOLOGY AND PATHOLOGY

The cause of the collagen diseases is not known. Several investigators have produced fibrinoid changes of connective tissue experimentally by mechanical

and by chemical means.[3] These observations tend to invalidate the supposition that hypersensitivity is the sole cause of collagenous degeneration. Indeed, it has been observed that undue significance should not be attached to the occurrence of fibrinoid changes in localized connective tissue collagen. Pathologically this is merely a form of degeneration, of unspecified cause, and it occurs in a wide variety of dissimilar diseases. This fact of course greatly diminishes the clinical usefulness of the term *collagen disease.* However, until a better term is devised and until more is known about the fundamental nature of the diseases in question, it is probably justifiable to continue the use of the makeshift. In this connection, it is to be noted that the microscopic findings are not merely of changes in the collagen fibers alone but of changes in the connective tissue elements as a whole.

Histologically, connective tissue consists of cellular elements and extracellular substances. The cellular elements consist of fibrocytes and fibroblasts, macrophages, lymphoid cells, mast cells and various other leukocytes. The extracellular substances are composed of an amorphous ground substance and three known types of fibers, collagenous, reticular and elastic. The basic lesion in the collagen diseases consists of a swelling of the interfibrillary ground substance as well as swelling of the fibers themselves. The location of these basic lesions and the type of response of the adjacent tissues are somewhat different in the different collagen diseases, and constitute the anatomic basis by which they may be at least partly distinguished.

Not all clinical subdivisions of the collagen diseases are clearly demarcated. Sometimes, at necropsy, lesions peculiar to or predominant in some of the different entities may be observed in one and the same subject. For example, a fatal case may show: (a) Chronic skin lesions, as in scleroderma, (b) atrophy of skin, and degeneration of muscle, as in dermatomyositis, (c) proliferation of endothelial capillary tissue, as in disseminated lupus erythematosus, (d) non-bacterial verrucous endocarditis,* (e) infiltration and dilatation of arterioles, as in periarteritis nodosa, (f) pericardial changes, as in rheumatoid infection, and (g) articular and tenosynovial changes, as in rheumatoid arthritis.

A case embodying all these diverse manifestations was reported by Kampmeier.[10]

Miale[14] mentioned that Krupp first emphasized a characteristic urinary finding in "visceral angiitis"; he found the pattern in 14 of 21 cases of periarteritis nodosa and disseminated lupus erythematosus. It consists of the simultaneous presence of elements usually characteristic of the early stages of nephritis (erythrocytes and erythrocytic casts), and elements usually seen in the chronic stage (broad casts, waxy casts, fatty casts, and "oval fat bodies"). This finding has been referred to as "telescopic urinary sediment."

*Non-bacterial verrucous endocarditis, as in Libman-Sacks syndrome,[11] is now known to be part of the changes occurring in disseminated lupus erythematosus.

CLINICAL TYPES AND SOURCE OF MATERIAL

The types of collagen disease to be discussed herein include periarteritis nodosa, generalized lupus erythematosus, dermatomyositis, and scleroderma. Only brief mention will be made of the two more common entities, rheumatic fever and rheumatoid arthritis.

The cases studied were obtained by a review of the files in the x-ray departments and the record rooms at the San Francisco Hospital and the Stanford University Hospital.† The period covered is approximately 15 years, a majority of the cases having been indexed in the last 10 years.

Periarteritis Nodosa (Polyarteritis)

Periarteritis nodosa is frequently and more correctly called polyarteritis as there is actually a widespread *poly-* rather than *peri*arteritis, affecting chiefly the medium-sized and smaller arteries of the body. Pathologically there is a degeneration of the collagenous tissue in the walls of the vessels, sometimes with necrosis of the media, rupture of the elastic lamina and infiltration of inflammatory cells and eosinophils into all the vascular layers. When this infiltration of the arterial coats is localized, or is followed by local fibrosis, or the development of small aneurysmal dilatations, nodular changes develop (giving rise to the term *nodosa*).

Clinically the signs and symptoms are determined more by the distribution of the involved arteries than by the disease process itself. Almost any clinical condition may be mimicked. However, a polysystemic involvement with chronic fever, leukocytosis, eosinophilia and secondary anemia suggests the condition, and is an indication for skin and muscle biopsy.

Radiologically, findings may or may not be present, depending on which systems happen to be involved, and also on the acuteness and degree of involvement. Cardiac enlargement and/or pericardial effusion occurs. The respiratory system may show massive symmetrical or non-symmetrical edema in severe acute cases. In others, small hazy shadows or non-confluent patches of edema (pulmonary hives) may be scattered throughout the lung fields, usually peripherally and at the bases.[1] Some observers[5, 17] have reported cases in which the nodulation was most pronounced centrally. In addition

†The authors are indebted to Dr. H. S. Kaplan for permission to review the latter.

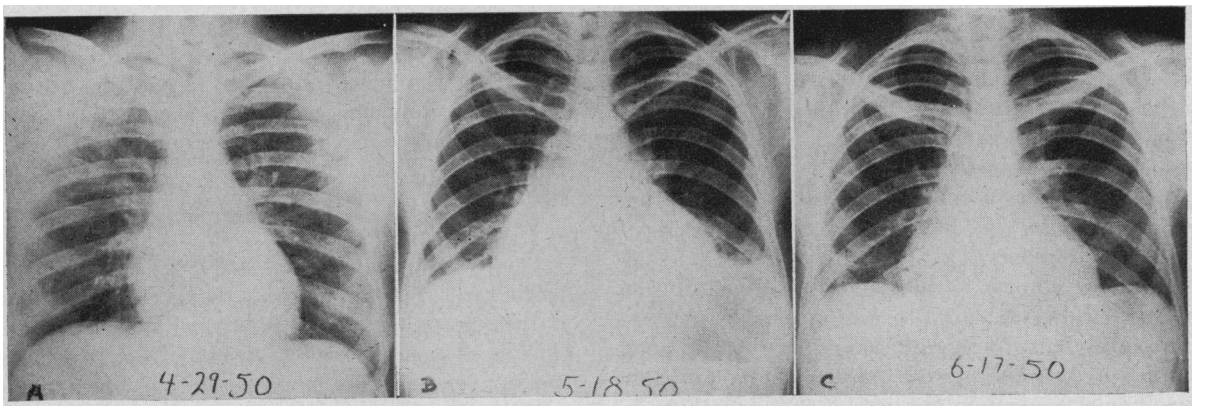


Figure 1.—Periarteritis nodosa. Acute pericardial and bilateral pleural effusions developed during a chronic illness of two years. Biopsy positive. The patient was a white woman 26 years of age with arthralgia, myalgia, fever and gangrene of tips of fingers and toes. *A.* Chest film negative; pericardial friction rub present. *B.* Pericardial and bilateral pleural effusions. *C.* Improvement; also improved clinically, under cortisone therapy.

to the nodular densities, the pulmonary linear markings may be accentuated, particularly the hilar and basal ones. Pleural effusion, secondary to pneumonitis or pulmonary infarction, is reportedly not uncommon.

X-ray examination of the abdomen is frequently requested since abdominal pain is one of the commonest early symptoms. A triad of myositis, abdominal pain and loss of weight has been referred to by some investigators. The abdominal films usually show either no abnormality or some collections of gas suggesting paralytic obstruction (so-called adynamic ileus). Very rarely, there may be a perforated ulcer, intestinal infarction or pancreatic necrosis. In one of the cases in the present study there were both intraperitoneal and retroperitoneal bleeding due to ruptured aneurysm of a small mesenteric vessel, secondary to "healed" arteritis. Hypertension was present, the blood pressure 200 mm. of mercury systolic and 140 mm. diastolic. The patient also had multiple duodenal ulcers.

Renal lesions are the commonest of all the systemic lesions, being present in 80 per cent of the cases.[13] Occasionally hypertension or hematuria may be so prominent that intravenous pyelograms are requested. These usually show either normal or decreased function.

The records of 29 cases of periarteritis nodosa were reviewed. In 28 of these, films of the chest were available and disclosed the findings shown in Table 1. It is to be noted that in some cases there was more than one abnormality observed (for example, pericardial, pleural and pulmonary lesions).

In one case, in which -ray films had shown cardiac enlargement, pulmonary congestion and pleural effusion, both polyarteritis and rheumatic heart disease (mitral and aortic stenosis with insufficiency) were noted at autopsy.

None of the x-ray findings noted in Table 1 are

TABLE 1.—*Observations in x-ray films of chest in 28 cases of periarteritis*

No evidence of disease		9
Evidence of disease		19
*Cardiac enlargement	4	
Pericardial effusion	4	
Pleural effusion	4	
Pulmonary changes	14	
Parenchymal nodules, patches, etc.	4	
Pulmonary congestion, passive	6	
Accentuated markings, ? arteritis	3	
Pulmonary edema, massive	1	

*In some of the cases in which "cardiac" enlargement was observed there may also have been some pericardial effusion.

diagnostic *per se* of periarteris nodosa, but the presence of pulmonary, pleural or cardiopericardial changes in a patient with involvement of other systems should cause one to bear the possibility of a collagen disease in mind.

In the 29 cases, adequate radiological records of systems other than the cardiorespiratory were limited. In two cases, hepatomegaly and in two cases splenomegaly were noted by physicians in the Department of Radiology. X-ray evidence of mild paralytic ileus was noted in one case, and in three there was peptic ulcer (one gastric and two duodenal). No cases of gross renal enlargement were recorded, but in one case poor function was shown by excretory urography. No bone changes were noted; in three patients there was x-ray evidence of articular disease (synovial thickening in two and rheumatoid arthritis in one). Biopsy or necropsy material compatible with the diagnosis of periarteritis nodosa was available in 17 out of the 29 cases. In seven cases biopsy reports were negative for periarteritis nodosa but the clinical evidence was outstanding and two of the patients died apparently of the disease.*

*Most of the histopathological studies referred to in connection with the cases reported in this paper were made by members of the staff of the Department of Pathology, Stanford University School of Medicine. In a few instances material was reported upon by members of the University of California staff at the San Francisco Hospital, to whom the authors are indebted.

The following are illustrative cases:

¶ A 26-year-old white woman with migratory pains in the joints, low-grade fever, myalgia and patchy gangrene of some of the fingers and toes was known to have had periarteritis nodosa for two years. Upon radiographic examination of the chest no abnormality was noted. Reexamination two and one-half weeks later showed small bilateral pleural effusions and pericardial effusion. A month later, after cortisone therapy, clinical and radiographic improvement was present. In this case there was acute development of pleural and pericardial lesions during the course of a chronic, multiple-system disease. Biopsy of skin and muscle was positive for periarteritis nodosa.

¶ The patient, a 63-year-old man, had had fainting spells of unknown cause for a few weeks, and pain and stiffness of the shoulders and knees since a fall one month before admittance to hospital. Initial x-rays of the chest showed only slight left ventricular enlargement. Two days later, films showed bilateral pleural effusion and pulmonary congestion. Clinically the patient had become acutely ill, with high fever (up to 103.1 degrees F.), but there was no evidence of cardiac failure. X-ray examination four weeks later showed clearing of the congestion and effusions, but the patient was failing generally. Abnormalities then were noted in the urine (the so-called telescopic sediment) and the possibility of "visceral angiitis" was considered. The patient recovered partially and was discharged. Biopsy of skin and muscle was reported negative.

¶ A 34-year-old white woman had had asthma for one year and numbness of the left leg and pain in the left foot for six months. She was found to have splenomegaly, eosinophilia and a renal lesion, with casts and cells. X-ray films of the chest showed pulmonary nodulation, fibrosis and emphysema. Biopsy of skin and muscle was reported negative. Pronounced clinical and radiological improvement occurred within three days after cortisone was started. The patient was discharged improved.

¶ A white longshoreman 45 years of age entered the hospital with chilliness, fever (101 degrees F.), mild cough, pain in the chest and dyspnea. He had dermatitis of two years' duration on the leg, with local ulceration. Pain in the right upper quadrant of the abdomen, pronounced enlargement of the liver and massive hematuria developed. The blood pressure was 180 mm. of mercury systolic and 80 mm. diastolic. The urea content of the blood was 27 mg. per 100 cc. The number of leukocytes was within normal limits. X-ray films showed clouding of the right upper lobe and of the left midlung field, interpreted as pulmonary edema. Moderate splenomegaly was noted on an abdominal film. Nine days after admittance the patient was clinically and radiologically improved. Biopsy was not performed. A year later, no abnormality was noted in an x-ray film of the chest.

¶ The patient was a 40-year-old white man with clinical diagnosis of rheumatoid arthritis. X-ray films showed cardiomegaly, predominantly left ventricular, and bilateral pleural effusion. The patient died shortly after examination, apparently from cardiac failure. Autopsy showed:

A. Diffuse collagen disease with
   1. Polyserositis (peritoneal, pleural and pericardial fluid)
   2. Rheumatic heart disease (aortic valve stenosis)
   3. "Wire-looping" of renal glomeruli (as in lupus erythematosus)
   4. Rheumatoid arthritis
   5. Periarteritis nodosa (of pulmonary, thyroid and testicular arteries)

B. Pulmonary emphysema (and fibrosis)

C. Generalized arteriosclerosis (coronary, aortic and renal).

In this case there was a combination of four types of "collagen" disease—periarteritis nodosa, lupus erythematosus, rheumatoid arthritis and rheumatic carditis.

Disseminated Lupus Erythematosus

Disseminated lupus erythematosus, or systemic lupus erythematosus, is a disease most commonly seen in women, and in the ages of 20 to 40. It is characterized by a cutaneous eruption, most often in the form of discoid lesions—with a butterfly distribution over the nose and cheeks—along with varying degrees of visceral manifestation, notably in kidneys, heart, spleen and lungs. The skin lesion is frequently photosensitive, being made worse by sunlight or ultraviolet light or such light-sensitizing drugs as the sulfonamides. Patients may have fatigue, arthralgia and fever. The laboratory findings include leukopenia, accelerated sedimentation rate, "telescopic" urinary sediment and the presence of so-called lupus erythematosus cells.[9] These cells, found only in this disease, are seen in various preparations of blood and bone marrow and are reportedly large leukocytes containing phagocytosed material resulting from lysis of the nuclei of other leukocytes.

Pathologically, there is predominant involvement of the smaller arteries and arterioles. Polyserositis is common, with pericardial lesions the most frequent. In the heart itself, lesions predominate in the valvular structures and the mural endocardium. The kidneys, when involved, tend to be enlarged. The glomerular vessels show the so-called "wire-loop" appearance due to eosinophilic thickening of the vascular loops within the glomeruli. Occasionally the renal changes resemble those of glomerulonephritis or periarteritis nodosa. Periarterial fibrosis may be seen microscopically in at least half of the cases. The lymph nodes are said also to be frequently involved, showing "free hematoxylin-staining bodies."[11]

Radiologically, abnormalities may be noted in the urinary and respiratory tracts. When a patient with hypertension has unusually large kidneys, the possibility of disseminated lupus erythematosus rather than a chronic glomerular nephritis must be considered. Patients with the latter condition tend to have small or contracted kidneys. Pulmonary involvement is remarkable for its frequency and its atypical course. Rakov and Taylor[16] and Foldes[6] described chronic interstitial pneumonitis which leads to atelectasis (due to interstitial edema and inflammation resulting in obliteration of some alveoli)—termed atelectasizing pneumonitis. These lesions are regarded as different from the ordinary pyogenic and fibrinous types of bronchopneumonia which so frequently complicate the terminal stages of lupus erythematosus.

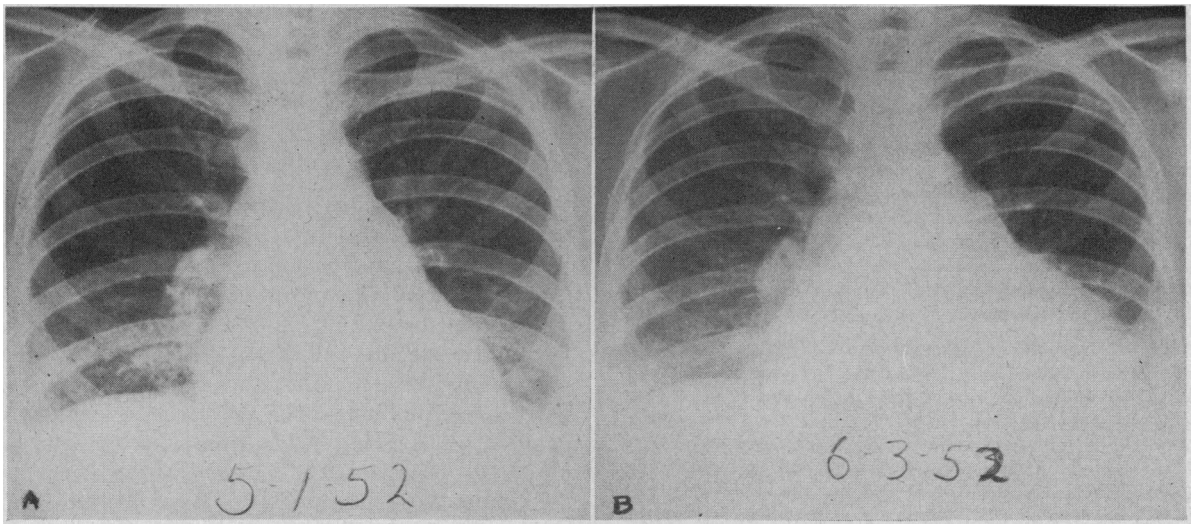


Figure 2.—Disseminated lupus erythematosus, showing right basal nodular densities, with pleural and pericardial effusions. The patient was a 25-year-old white woman. Peripheral arthritis, hematuria, fever and pericardial friction rub, three days. *A.* Small nodular densities, right base, small bilateral pleural effusions, enlarged heart-vessel shadow. *B.* Right basal nodulations obscured or not present; effusions increased. Discharged unimproved.

Thorell[20] reviewed the x-ray films in 15 cases of disseminated lupus erythematosus and found that in eight cases there were pleural or pulmonary parenchymal changes, or both. The pleural effusions were generally small; the pleural thickening more or less irregular. These pleural changes varied in extent in relatively short periods. The parenchymal changes consisted of small areas or patches of increased density, mostly subpleural, especially in early and moderately advanced cases. Thorell used different oblique projections to bring out the subpleural location of the lesions. He expressed the opinion that a combination of pleural and subpleural change ought to lead to the correct diagnosis even if the changes in themselves were not characteristic.

In the series herein reviewed, pleural and pericardial effusions were the commonest findings in lupus erythematosus. The pulmonary parenchymal changes varied from localized accentuated markings, nodules and patches, to extensive edema.

The records of 35 cases of lupus erythematosus, in 32 of which chest films were available, were reviewed (Table 2).

As far as anatomic sites other than those mentioned in Table 2 are concerned, radiological findings were limited. In one case hepatomegaly was reported; in two cases, ascites was noted. No gastrointestinal lesions were detected. In one case, slight osteoporosis of the hands was noted. While there was clinical evidence of joint disorder in many cases, there were no reports of roentgen studies of the joints (largely because examination was not regarded as necessary by the ward physician).

Biopsy or necropsy material compatible with the diagnosis of disseminated lupus erythematosus was available in 24 out of the 35 cases. In two cases biopsy reports were negative.

TABLE 2.—*Observations in x-ray films of the chest in 32 cases of disseminated lupus erythematosus*

No evidence of disease		11
Evidence of disease		21
Cardiac enlargement	5	
Pericardial effusion	5	
Pleural effusion	13	
Pulmonary changes	10*	

*The pulmonary changes consisted of accentuated basal bronchovascular markings in two instances, of nodular or patchy pulmonary densities (possibly edema) in six instances, and of diffuse pulmonary density (edema) in two instances.

The following are illustrative case reports:

¶ A white girl 19 years of age had facial rash of butterfly shape, fever, pain in the joints of six months' duration, and generalized edema (nephrotic syndrome?) of four weeks' duration. X-ray films of the chest showed a small amount of fluid in the costophrenic sulci. (This minimal, bilateral effusion, without other roentgen evidence of chest disease, is one of the more suggestive findings of disseminated lupus erythematosus—in patients with concomitant clinical symptoms.) Biopsy was not performed.

¶ A 13-year-old boy entered the hospital with high fever and weakness, splenomegaly and lymphadenopathy of two months' duration and a butterfly facial rash that had been present a month. Slightly accentuated pulmonary markings were noted in x-ray films of the chest. Three days later films taken at bedside showed bilateral pneumonitis, and six days later the patient died. At autopsy disseminated lupus erythematosus was observed, and also bilateral atypical lobar pneumonia with features suggesting the anaphylactic pneumonia reported by Rich[18] as occurring in rheumatic fever and in patients with sulfonamide sensitivity.

¶ A 25-year-old housewife had peripheral arthritis with migratory pain in the joints. An episode of hematuria had occurred a month before admittance to hospital, and fever and a pericardial friction rub had been present for three days. X-ray films showed some small nodular densities in

the right lower lung field, small bilateral pleural effusions and cardiac enlargement. No abnormality was noted in an intravenous pyelogram. Biopsy was not performed.

Polysystemic manifestations such as were noted in this case (articular, renal, pericardial, pulmonary), plus the small bilateral pleural effusions, are highly suggestive of a collagen disease. Cases such as the present one, in which there is no development of skin lesions during the course of disseminated lupus erythematosus, are few. In a few others the skin lesions may appear only fleetingly.

¶ A 15-year-old girl had painful, swollen joints and fever. X-ray films of the chest showed a "water-bottle" shaped heart suggesting pericardial effusion (this was confirmed by fluoroscopy). Minimal bilateral pleural effusion also was noted. Examination 18 days later showed a pronounced decrease in the size of the heart; the pleural effusions were unchanged. The clinical diagnosis was disseminated lupus erythematosus. Biopsy was not performed.

¶ The patient was a 36-year-old white man with a history of chorea at age 12. Two and one-half years before admittance to hospital, a butterfly rash developed, then hematuria and fever, weakness and fatigue. Some ten months before the x-ray and autopsy examinations reported herein were carried out, the patient was hospitalized and disseminated lupus erythematosus was diagnosed. The blood pressure at that time was 170 mm. of mercury systolic and 96 mm. diastolic. After several months, pronounced orthopnea and minimal edema developed and the blood pressure varied from 160 mm. of mercury systolic and 90 mm. diastolic to 200 mm. and 110 mm. respectively. The patient died of cardiac failure. X-ray films taken ten days before death showed cardiac enlargement. At autopsy chronic glomerular nephritis (without evidence of disseminated lupus erythematosus) and lesions of the spleen consistent with disseminated lupus erythematosus were noted. There was microscopic evidence of active rheumatic lesions. In this case there was a combination of "collagen" diseases.

Dermatomyositis

Dermatomyositis, the rarest of the collagen diseases, is characterized by non-suppurative inflammation of the skin, the subcutaneous tisssues and the skeletal muscle. There also may be inflammatory changes in the vessels, the myocardium and the muscles of deglutition. Little is known of the radiological features. In the present series there was only one autopsy-proven case, and in that case cloudy swelling of the myocardium and congestive failure was noted at necropsy. X-ray films of the chest taken a year before death showed the heart slightly larger than normal, but several weeks before death the heart-vessel shadow was normal in size. The lungs were clear.

Scleroderma

Scleroderma is a polysystemic disease, with fairly well known roentgen findings. Large series of cases have been reported in the literature, one of the most comprehensive, from the radiological viewpoint, being that by Pugh.[15] Table 3, prepared from data in the literature and the authors' observations, is believed to summarize the more important radiological changes in this disease.

TABLE 3.—*Summary of the radiological findings in scleroderma*

- A. Gastrointestinal Tract
  - 1. Esophagus
    - a. Loss of peristalsis due to rigidity
    - b. Variable degrees of dilatation
    - c. Occasional narrowing of distal esophagus
    - d. Occasional shortening of esophagus
  - 2. Stomach
    - a. Peristalsis may be decreased
    - b. Hiatus hernia may develop
  - 3. Small Bowel
    - a. Peristalsis decreased or absent
    - b. Widening, especially of duodenum and jejunum; this may be segmental
  - 4. Colon
    - a. Peristalsis decreased
    - b. Segmental narrowing
- B. Lungs
  - 1. Diffuse or localized fibrosis
  - 2. Diffuse or localized nodulation
  - 3. Subpleural "cystic disease" (basal)
  - 4. Calcification (calcinosis)
- C. Heart
  - 1. Decreased amplitude of excursion
  - 2. Heart may be small, normal or large
- D. Phalanges
  - 1. Absorption of distal phalanges in advanced cases
  - 2. Occasional increased density of phalanges
  - 3. Occasional synostosis, distal and middle phalanges
- E. Soft Tissues
  - 1. Calcinosis—fairly frequent and often accompanies phalangeal absorption
    - a. Varies from "sand" to plaques
    - b. Usually in pressure areas: fingertips, elbows, ischial tuberosities
    - c. Usually seen only where there is cutaneous sclerosis.
- F. Teeth
  - 1. Uniform widening of the periodontal spaces (reported in 7 per cent of cases)

Roentgen studies carried out in 10 microscopically proven cases of scleroderma were reviewed. In five of them there was roentgenographic evidence of some degree of small bowel abnormality. In one case, the first suggestion of scleroderma was made by one of the authors upon examination of a film of the small bowel. It is the authors' impression that the small bowel involvement often starts as a dilatation of the third portion of the duodenum, and then progresses distally. In one case, however, the changes in the bowel appeared to start with areas of narrowing. Three of the five patients with scleroderma involving the small bowel died.

One of the ten patients with proven scleroderma had pulmonary disease:

¶ A Chinese man 75 years of age had loss of weight from 150 to 116 pounds, pronounced weakness, dyspnea, edema at the ankles and a cough productive of white, frothy phlegm. The skin of the face and fingers appeared drawn, tense and shiny. The patient died of ruptured diverticulitis of the midascending colon eight days after treatment with corticotropin was started. X-ray films of the chest five months before death showed minimal prominence of the lower lobe pulmonary markings and slight cardiac enlarge-

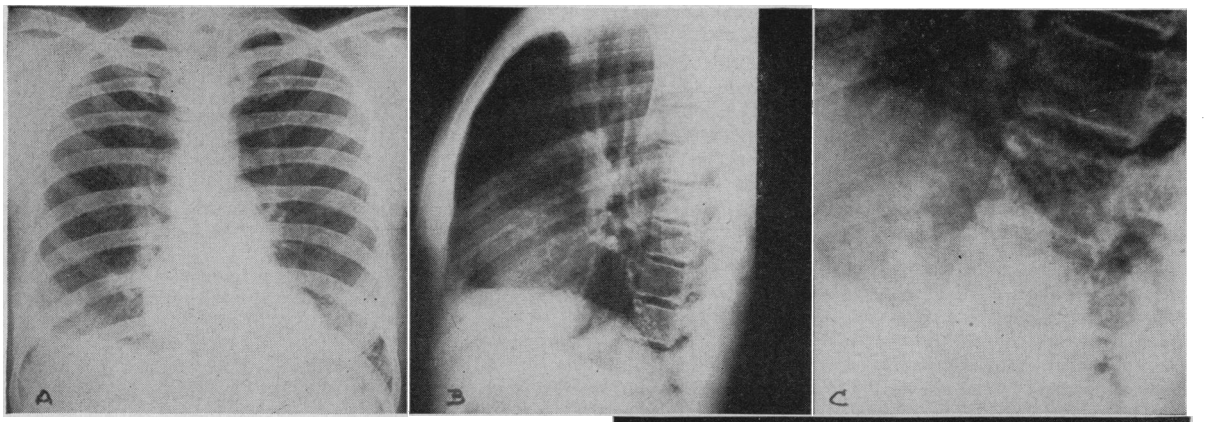
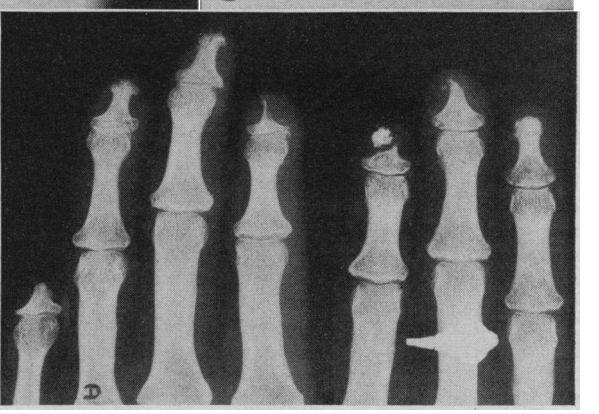


Figure 3.—Scleroderma, with cystic disease of the lung bases. The patient, a Negro woman 30 years of age, had had scleroderma for twelve years. *A.* Mottled radiolucencies (? cysts) in lung bases. *B.* Lateral view of same. *C.* Detail view of cystic appearance. *D.* Tuft absorption and calcinosis.



ment. Examination three days before corticotropin therapy was begun showed hazy widening of the pulmonary markings throughout both lung fields, with a few areas of small (2 to 3 mm.) hazy nodules along the course of these markings. The changes were more evident in the right upper lobe, where one patchy density (1.5 x 3 cm.) also was present. The left costophrenic sulcus was blunted by fluid.

Among several clinically diagnosed cases of scleroderma was one in which there were subpleural cystic changes. The patient was a Negro woman 30 years of age with definite scleroderma for 12 years. X-ray films of the chest showed a peculiar "spongy" appearance in the bases of the lungs, presumably due to cystic changes as described by Getzowa[7] in two cases. Getzowa considered the changes examples of "cystic and compact pulmonary sclerosis." The "cysts" varied from pinhead size up to 1.5 cm. in diameter. In only one of the two cases was there concomitant extensive fibrosis. The cystlike changes were believed to be due to a disappearance of alveolar tissue in the lung secondary to lysis of the alveolar walls and progressive sclerosis. This sclerosis is reportedly on the basis of "a hyaline process involving the alveolar walls, accompanied by the disappearance of capillaries, superimposed on a generalized, diffuse simple fibrosis of the alveolar walls."

Reports of other cases illustrative of features of scleroderma follow:

¶ A white woman, 42 years of age, was admitted to hospital with a history of attacks of abdominal pain, nausea, vomiting and diarrhea for about 18 months. She had had peripheral vascular changes of the Raynaud's disease type for two years. About eleven months before entry she had had cholecystectomy; chronic cholecystitis was reported.

X-ray examination revealed widening and delay in the third portion of the duodenum and proximal small bowel. Fluoroscopically, the esophagus showed sluggish passage of the barium. No abnormalities were noted in x-ray films

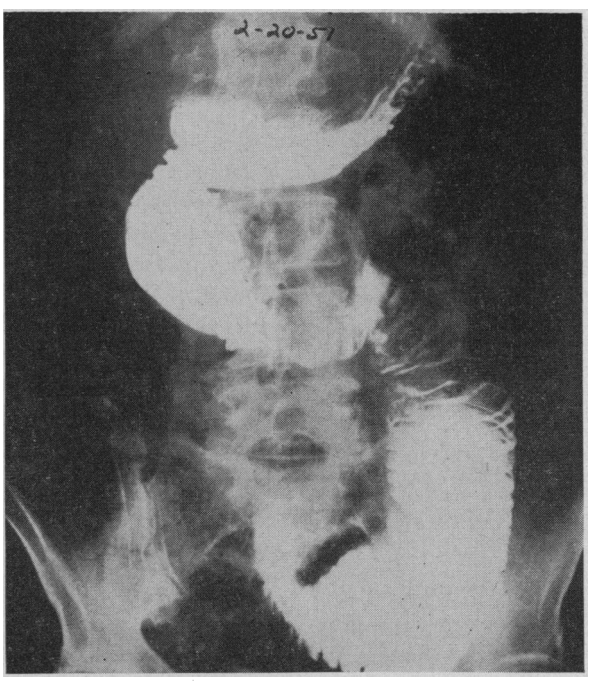


Figure 4.—Scleroderma, with involvement of small bowel. The patient was a 42-year-old white woman. Raynaud's phenomenon had been present two years. There had been attacks of abdominal pain, nausea, vomiting and diarrhea for one and one-half years. Autopsy, six months after examination, showed generalized scleroderma. X-rays showed upper small bowel dilation and delay.

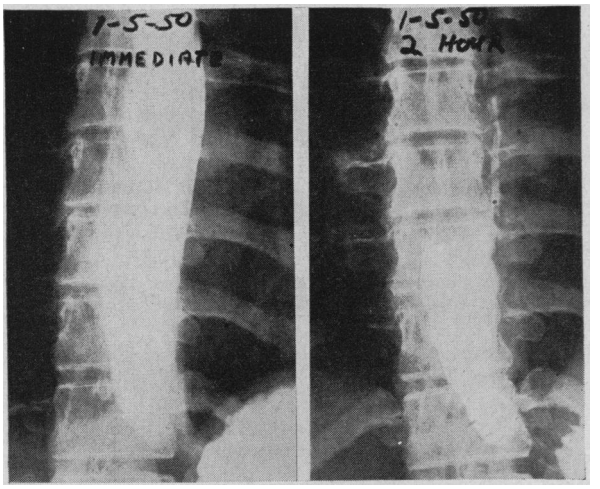


Figure 5.—Scleroderma, with esophageal involvement. The patient was a white woman 36 years of age with onset of disease three years previously, and with recent nausea, anorexia and dysphagia. Biopsy of skin showed scleroderma. X-ray examination showed esophageal widening, decreased peristalsis and pronounced delay.

of the chest and hands. Six months later the patient died "from asthenia," and at autopsy generalized scleroderma was observed.

A 36-year-old white woman had sclerodermal symptoms for three years, starting as pain and stiffness in the extremities, followed by Raynaud's phenomenon. About one month before admittance to hospital, nausea, anorexia and dysphagia occurred. X-ray examination showed esophageal involvement, with widening, decreased peristalsis and pronounced delay in emptying. A biopsy of skin showed changes interpreted as scleroderma. When the patient was observed two and one-half years later, only slow progression of the disease was shown.

A 46-year-old Greek woman had the onset of scleroderma 15 years before admittance to hospital and dysphagia had been present for twelve years. X-ray examination showed esophageal and duodenal involvement, with widening and delay in each site. Calcinosis was noted in the soft tissues of the fingertips and prepatellar areas. Changes noted in skin biopsy were interpreted as scleroderma. The general health of the patient three years later was relatively good.

Rheumatic Fever and Rheumatoid Arthritis

Acute rheumatic fever is regarded as a collagenous degeneration which localizes selectively in the heart. The changes may be found in many other organs, as shown by the arthritic, dermal, serosal, intestinal and pulmonary manifestations of the disease. In the acute fulminating form of the disease, pulmonary complications are reportedly found in as high as 50 per cent of cases.[8] "Rheumatic pneumonitis" has no specific diagnostic features in our experience. Pericarditis is not uncommon. The involved joints tend to show only articular and periarticular swelling.

Rheumatoid arthritis is frequently complicated by myositis, neuritis and arteritis, as demonstrated in 70 per cent of muscle biopsies by Traut and Campoine.[21] Traut also stated that the biopsies showed aggregates of lymphocytes, epithelioid cells and plasma cells somewhat similar to those in dermatomyositis, lupus erythematosus and scleroderma. Pericarditis is the only unusually frequent cardiac complication, being especially common in juvenile rheumatoid arthritis (Still's disease). In addition, pneumonitis and pleuritis may occur along with the inflammatory reaction in the joints, but is rare. The x-ray findings in the bones and joints of patients with rheumatoid arthritis are well known.

DISCUSSION

Collagen diseases constitute an interesting group of disorders from the clinical side because of diagnostic and therapeutic challenge, from the pathological viewpoint because of recent interest in the intercellular substances, and from the radiological viewpoint because of their widespread but unfortunately non-specific nature. The latter is particularly true of the pulmonary manifestations of the collagen diseases. The authors feel that diagnostic possibilities, slim though they are, are enhanced by an awareness of these conditions, plus a knowledge that the patient has a polysystemic disease. It is desirable that radiologists, as clinicians, be able occasionally to suggest the consideration of one of these diseases, on logical grounds, and be cognizant of the further studies, clinical, laboratory or pathological, required to confirm the diagnosis.*

From a review of radiological findings in the present series, the authors have come to believe that pulmonary changes occur more frequently in periarteritis nodosa and disseminated lupus erythematosus than one would gather from the literature. Further, a survey of the histories of over 75 patients with established or clinically diagnosed collagen disease led to the distinct impression that peptic ulcers occur with relatively greater frequency in persons with these conditions than in other patients in hospitals in general.

In studying a patient for possible collagen disease it is desirable that particular attention be paid to the following structures: The skin and muscles, the heart and pericardium, the lungs and pleura, the abdomen and intestinal tract, the kidneys, and the bones and joints.

The skin and muscles may show microscopic evidence of involvement in any of the four types of collagen disease herein discussed—periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis and scleroderma. Histopathologic changes are reportedly fairly decisive in all except dermatomyositis, about which not enough is yet known; they are

*At the same time, it is believed that the term "collagen" disease is one of high abstraction, to be modified or abandoned as soon as advances in knowledge of the cause and of the fundamental nature of these conditions permit.

said to be most clear-cut in periarteritis, but there is divergence of opinion as to the clarity of changes in scleroderma.

The cardiac and pleuropulmonary changes are legion and non-specific. Pericardial effusion, cardiac enlargement, pleural effusion, pulmonary nodular changes and variable degrees of pulmonary edema or fibrosis may occur. These changes may be reversible.

Abdominal distention, with paralytic obstruction, may occur in periarteritis nodosa and disseminated lupus erythematosus, as also may renal enlargement.

The intestinal tract changes are most conspicuous in scleroderma, notably in the esophagus and small bowel (variable degrees of rigidity, dilation and narrowing occur in about 50 per cent of cases).

The articular and osseous changes occur in periarteritis, lupus and especially scleroderma. Radiologically, they are characteristic only in the latter condition. Calcinosis is also confined largely to this disorder.

450 Sutter Street.

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